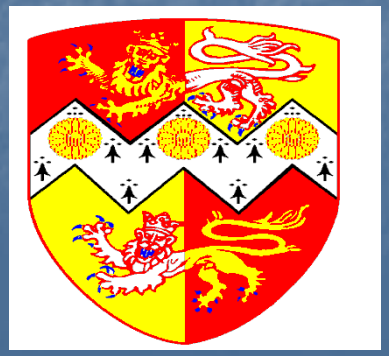
East Anglian Retinal Society
An Introduction to and Update in Diabetes

Dr Ketan Dhatariya MBBS MSc MD MS FRCP
Consultant in Diabetes and Endocrinology
Norfolk and Norwich University Hospital NHS Trust



What is Diabetes Mellitus?

"A complex metabolic disorder characterised by chronic hyperglycaemia resulting from defects in insulin secretion or insulin action, or both"

First described in 1550 BC

Two Main Types

- Type 1
  - Autoimmune destruction of the β cells of the Islets of Langerhans in the pancreas. This leads to an absolute insulin deficiency. Insulin treatment is therefore mandatory
  - Previously known as IDDM or juvenile onset diabetes

Two Main Types

- Type 2
  - Impaired insulin action (insulin resistance) and eventually, impaired insulin secretion as well
  - Usually treated with oral medication initially, then may move onto insulin
  - Formerly known as NIDDM or maturity onset diabetes

Other Types

- Gestational diabetes
- Drug induced diabetes
- Genetic disorders
- Pancreatic disease

How is the Diagnosis Made (1)?

Plasma glucose concentration following a 75 g oral glucose load (mmol/L)	Fasting plasma glucose concentration (mmol/L)		
	< 6.1	> 6.1-6.9	≥ 7.0
<7.8	Normal	Impaired fasting glycaemia	Diabetes
7.8-11.0	Impaired fasting glycaemia	Impaired fasting glycaemia	Diabetes
≥ 11.1	Diabetes	Diabetes	Diabetes

How is the Diagnosis Made (2)?

- However, from earlier this year, HbA1c was also added to the diagnostic criteria – with > 48 mmol/mol (6.5%) being diagnostic of diabetes
- There are several issues with this, but it is a done deal

Familial Risks – Type 1

- If neither parent = 1 in 250
- If mother has it = 1 in 50 – 100
- If father has it = 1 in 12
- If 1 sibling has it = 1 in 15 – 30
- If 1 sibling and 1 parent has it = 1 in 10
- If both parents have it = 1 in 3

Familial Risks – Type 2

- If neither parent has type 2 diabetes = 10%
- If 1 parent has it = 20 – 30%
- If 1 sibling has it = 40%
- If both parents have it = 70%
- If an identical twin has it = 80 – 100%

Epidemiology

- The 2008/9 National Diabetes Audit found the prevalence of diabetes to be 4.13% in England and Wales, however 2010 QOF data showed it was 5.4%
- ~90% of whom have Type 2 diabetes
- Lifetime risk of developing diabetes is about 10%

The NHS Information Centre, National Diabetes Audit Executive Summary 2010
Diabetes UK 2011

Clinical Features

	Type 1	Type 2
Age at Onset (years)	< 40	> 40
Duration of Symptoms	Days or Weeks	Years
Body Weight	Normal or Low	Normal or High
Ketones	Yes	No
Insulin Mandatory?	Yes	No
Autoantibodies	Yes	No
Complications at Diagnosis	No	Up to 20%
Family History?	No	Yes
Other Autoimmune Diseases?	Yes	No
Percentage of cases	10%	90%

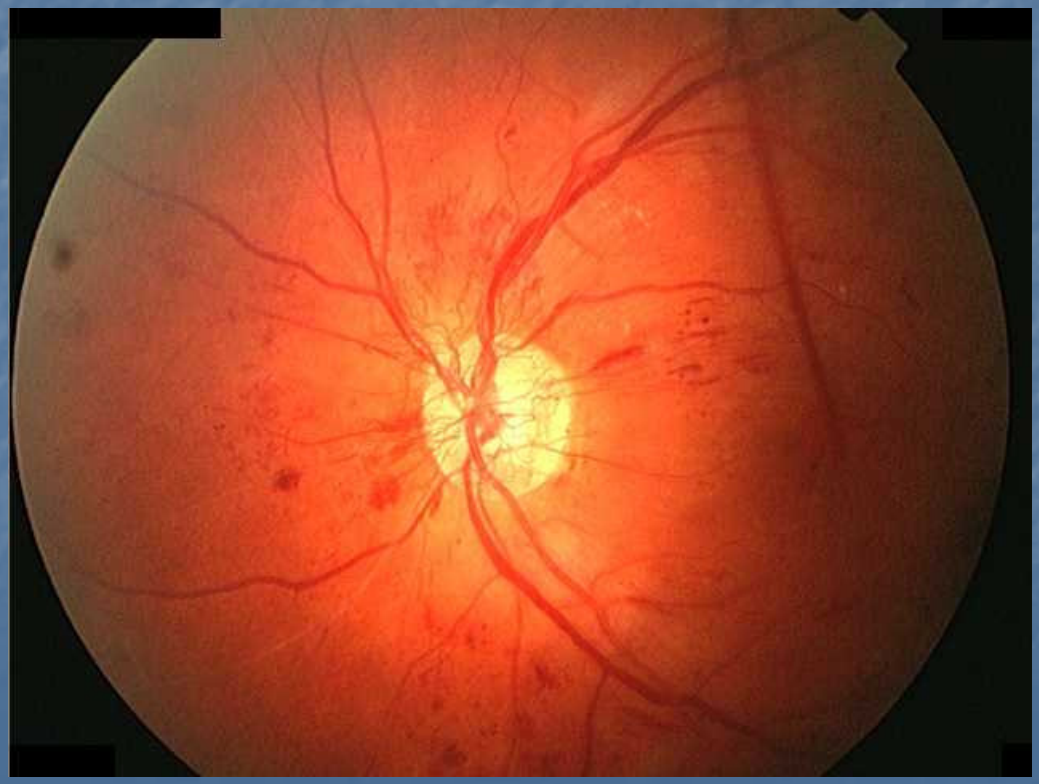
Why is it Important?

- Poorly controlled diabetes leads to accelerated cardiovascular morbidity and mortality
- A combination of microvascular and macrovascular disease

Thom T et al Circulation 2006;113(6):e85-151

Microvascular Disease

- Diabetic retinopathy – the commonest cause of blindness in the developed world



Diabetes and Eyes: Some History

- In the 1970's and 1980's diabetes was the leading cause of severe visual impairment
- People with diabetes were 25 times more likely to have a VA of 20/200 in their best eye due to
  - Haemorrhage
  - Tractional detachment of the macula due to proliferative diabetic retinopathy
  - Macular oedema
  - Cataract
  - Glaucoma

Klein R & Klein BE Diabetes 2010;59(8):1853-1860

Some History

- There was no definitive evidence that achieving good glycaemic control would actually result in less diabetic retinopathy
- Also, technology was not of a standard to allow easy optimisation of control
- In the early 1970's the efficacy of photocoagulation had not yet been demonstrated
- Vitrectomy was in its developmental stages

Klein R & Klein BE Diabetes 2010;59(8):1853-1860

The relationship Between Glycaemic Control and Retinopathy

- In 1978 Kelly M West wrote "The extent to which the level of hyperglycaemia determines the risk of retinopathy is not at all clear. This is the most important issue at hand and deserves high priority in epidemiologic research"

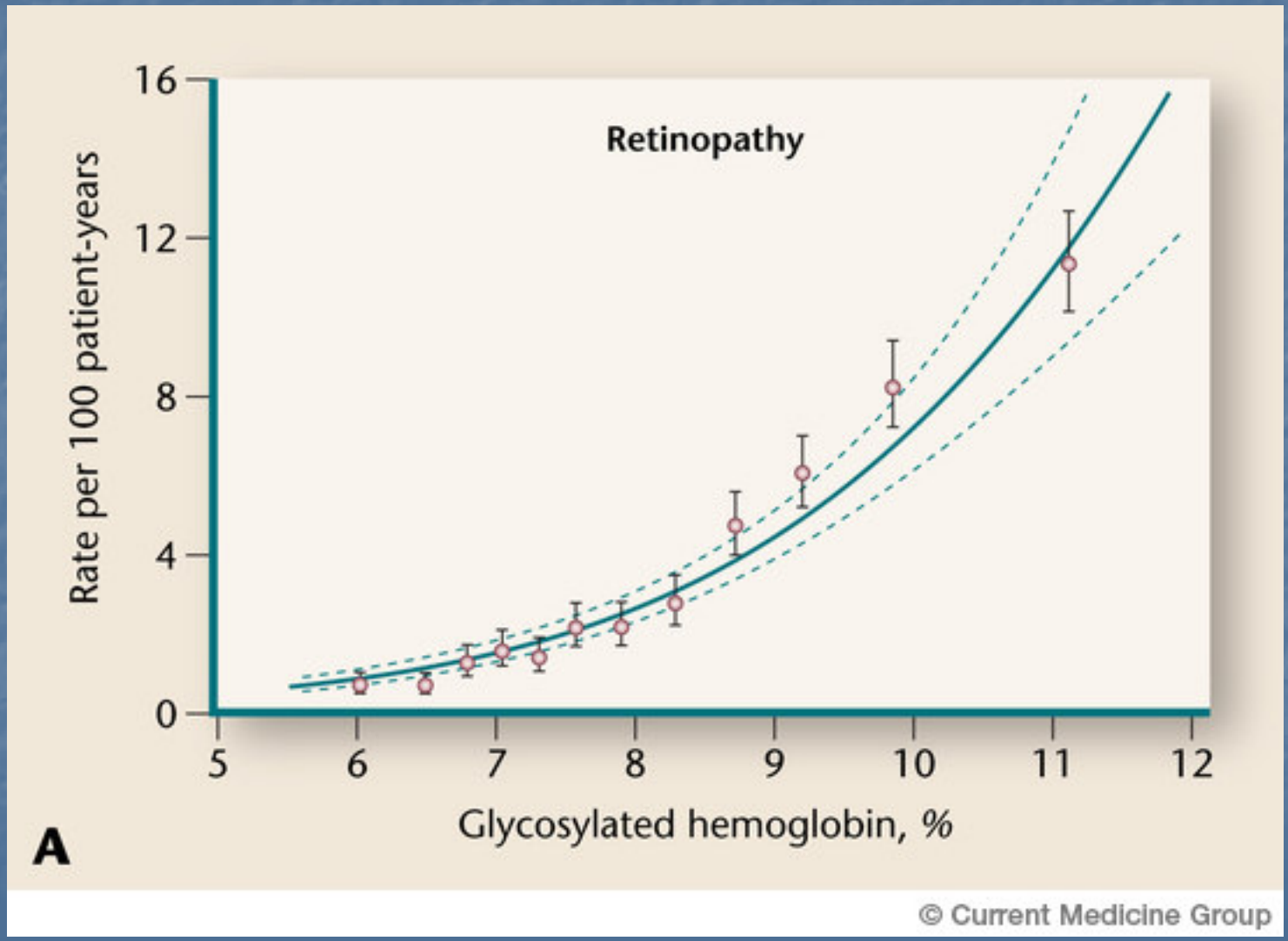
West KM. 1978. *Epidemiology of Diabetes and Its Vascular Lesions* . Elsevier, NY

WESDR

- It was the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) cohort data that first demonstrated a relationship between glycaemic control and the risk of retinopathy

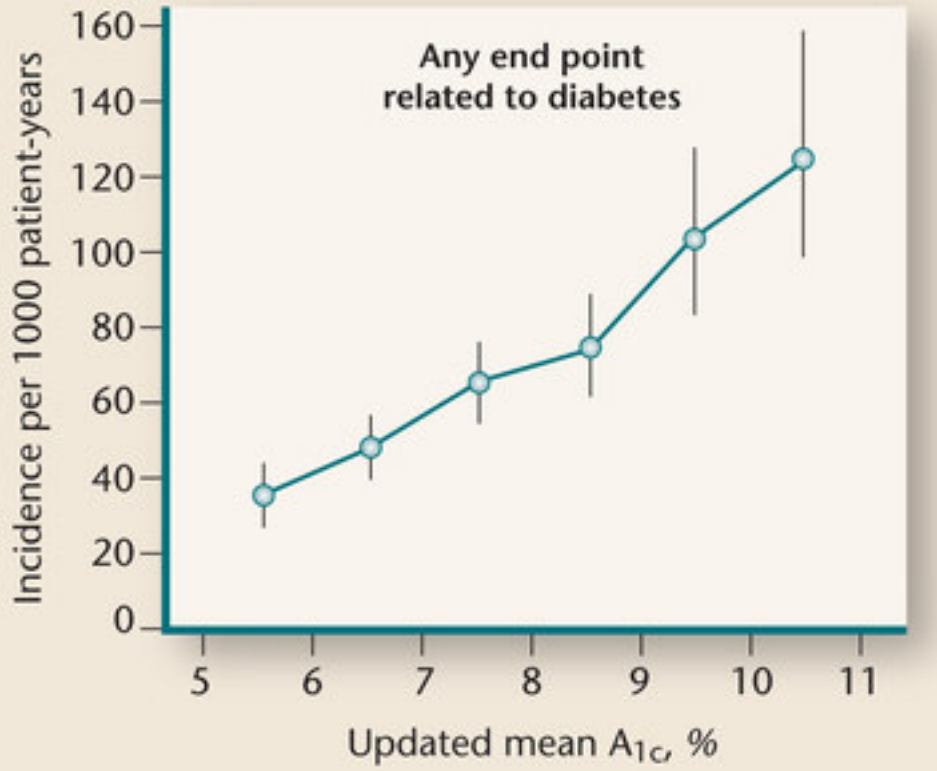
Klein R et al JAMA 1988;260:2864-2871

Retinopathy and Glycaemic Control



DCCT Research Group NEJM 1993;329(14):977-986

Glycaemic Control is Important



Reduction in risk per 1% reduction in A_{1c} (9 mmol/mol)

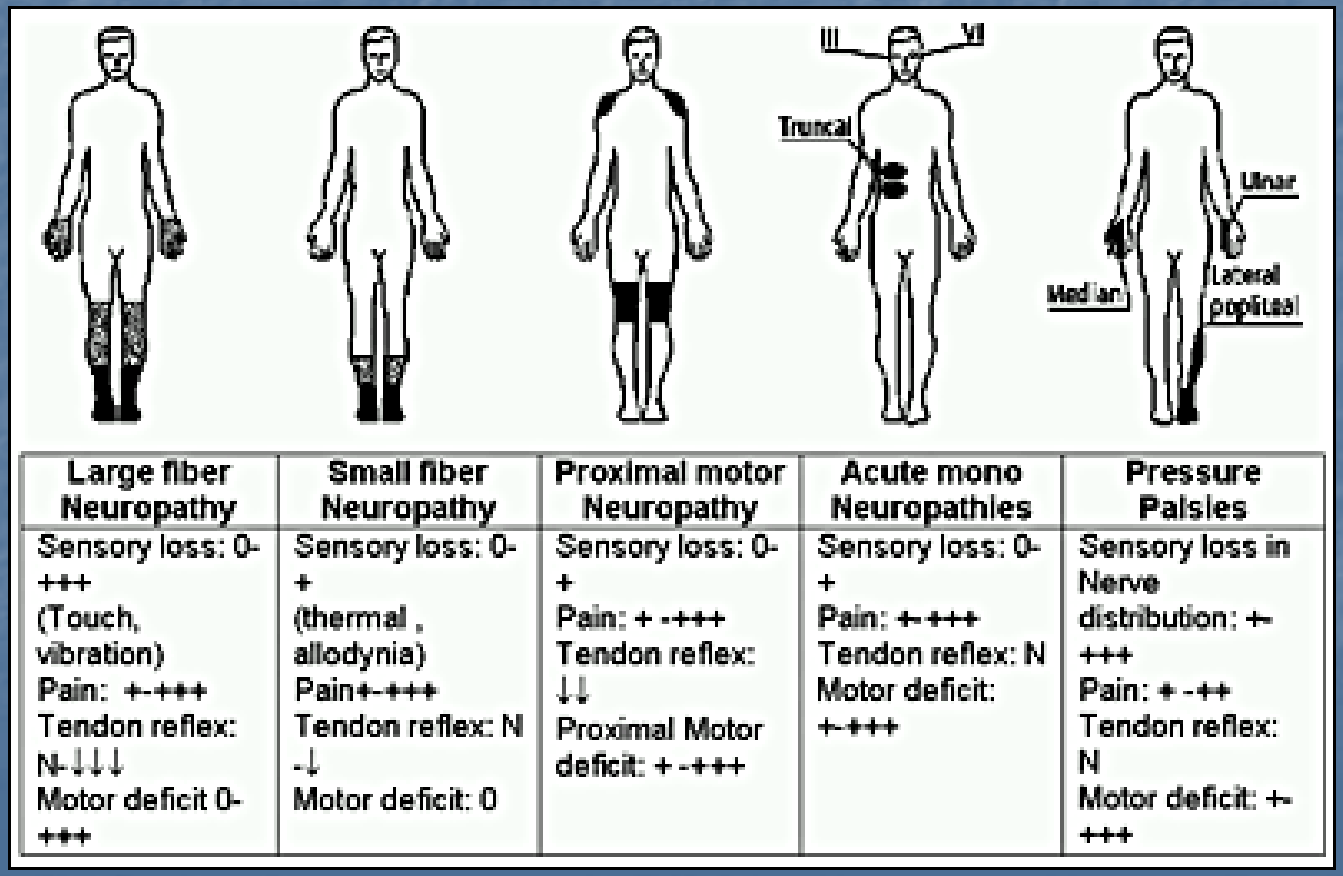
- Overall: 21%*
- Diabetes mortality: 21%*
- MI: 14%
- Stroke: 12%†
- Microvascular: 37%*
- Heart failure: 16%†
- Cataract extraction: 19%*
- Amputations or PVD death: 43%*

* $P < 0.0001$.
† $P < 0.05$.

UKPDS Lancet 1998;352(9131):837-853

Microvascular Disease

- Neuropathy



Large fiber Neuropathy	Small fiber Neuropathy	Proximal motor Neuropathy	Acute mono Neuropathies	Pressure Palsies
Sensory loss: 0-+++ (Touch, vibration) Pain: +-+++ Tendon reflex: N-↓↓↓ Motor deficit 0-+++	Sensory loss: 0-+ (thermal , allodynia) Pain+-+++ Tendon reflex: N -↓ Motor deficit: 0	Sensory loss: 0-+ Pain: + -+++ Tendon reflex: ↓↓ Proximal Motor deficit: + -+++	Sensory loss: 0-+ Pain: +-+++ Tendon reflex: N Motor deficit: +-+++	Sensory loss in Nerve distribution: +-+++ Pain: + -++ Tendon reflex: N Motor deficit: +-+++

Microvascular Disease

- Combinations of neuropathy and ischaemia

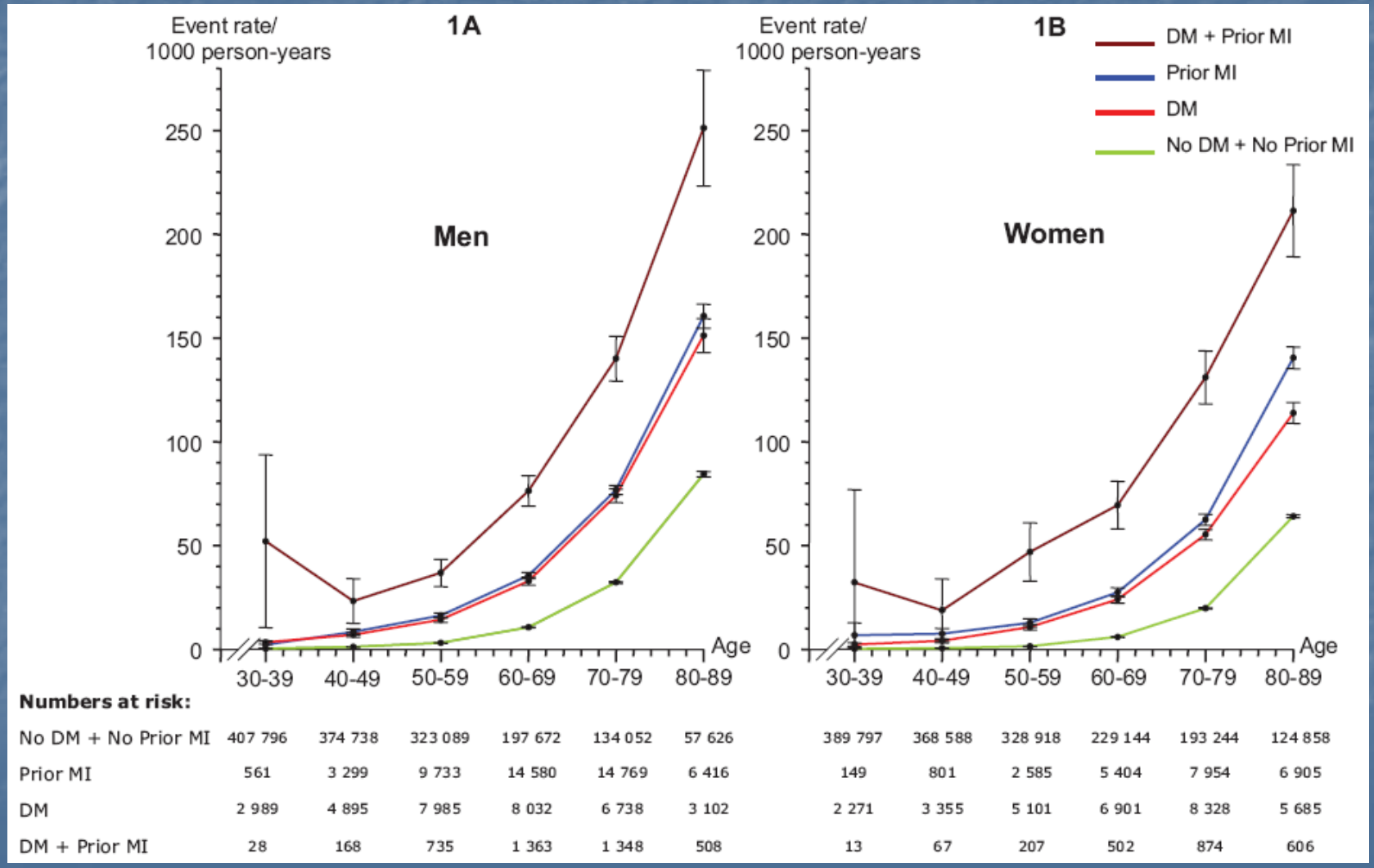
Microvascular Disease

- Nephropathy
  - Diabetes is the commonest cause of End Stage Renal Disease in the developed world

Macrovascular Disease

- Stroke
- Myocardial infarction

Data From 3.3M Danes

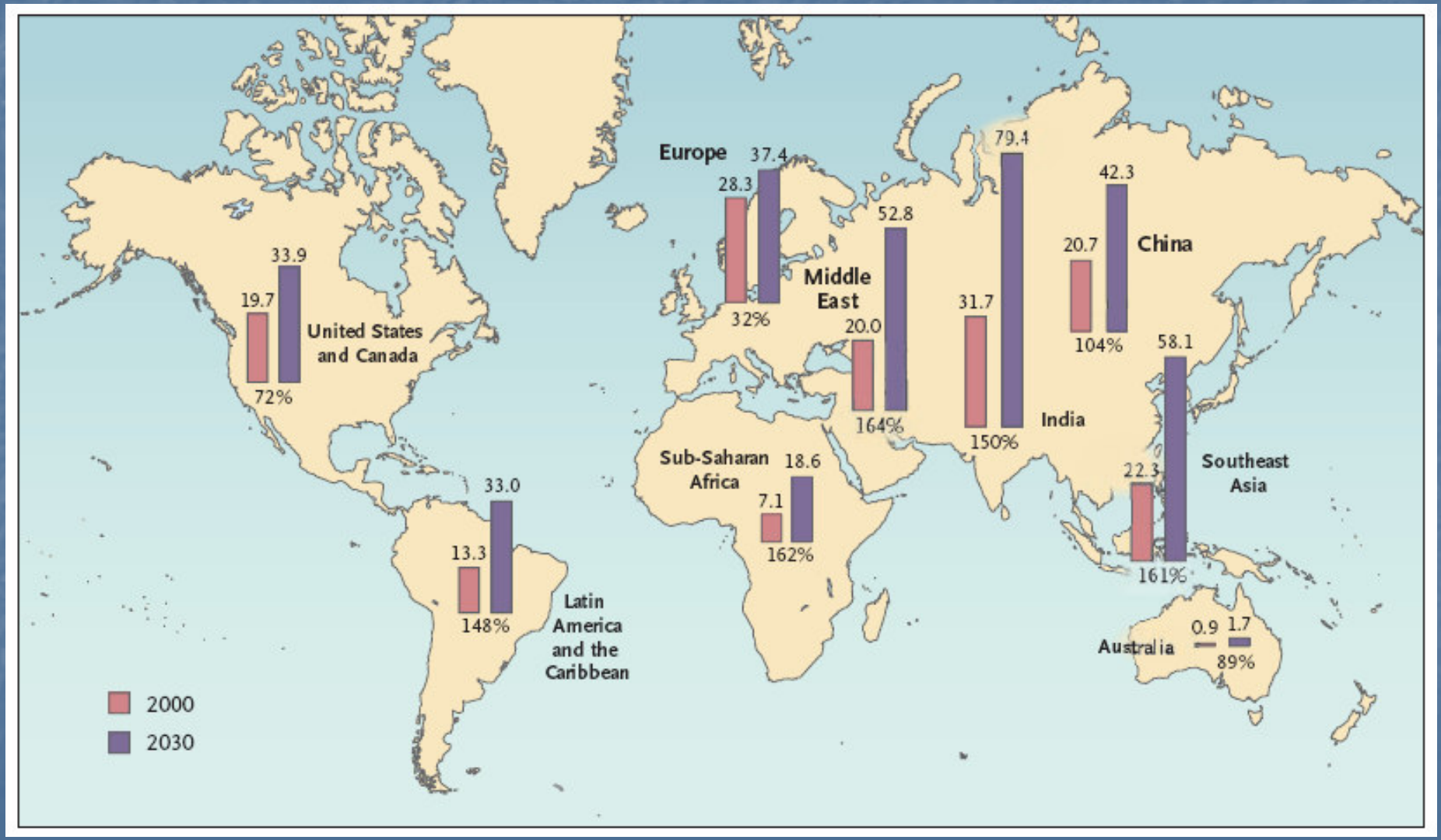


Numbers at risk:

No DM + No Prior MI	407 796	374 738	323 089	197 672	134 052	57 626	389 797	368 588	328 918	229 144	193 244	124 858
Prior MI	561	3 299	9 733	14 580	14 769	6 416	149	801	2 585	5 404	7 954	6 905
DM	2 989	4 895	7 985	8 032	6 738	3 102	2 271	3 355	5 101	6 901	8 328	5 685
DM + Prior MI	28	168	735	1 363	1 348	508	13	67	207	502	874	606

Schramm TK et al Circulation 2008;117:1945-1954

The Global Burden

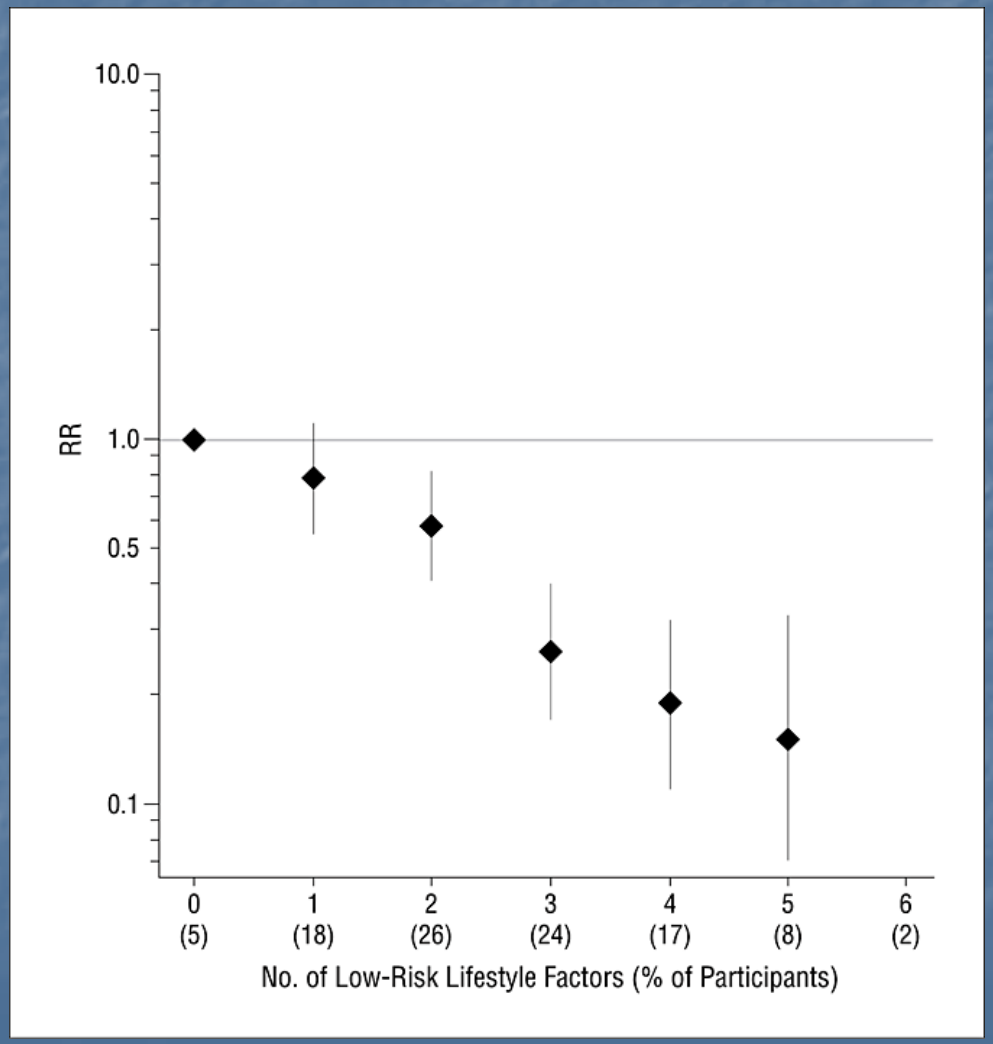


Millions of cases of diabetes in 2000 and estimate of 2030 and percentage change shown

The Global Burden

- Diabetes related healthcare costs account for about 10% of all health expenditure in developed nations

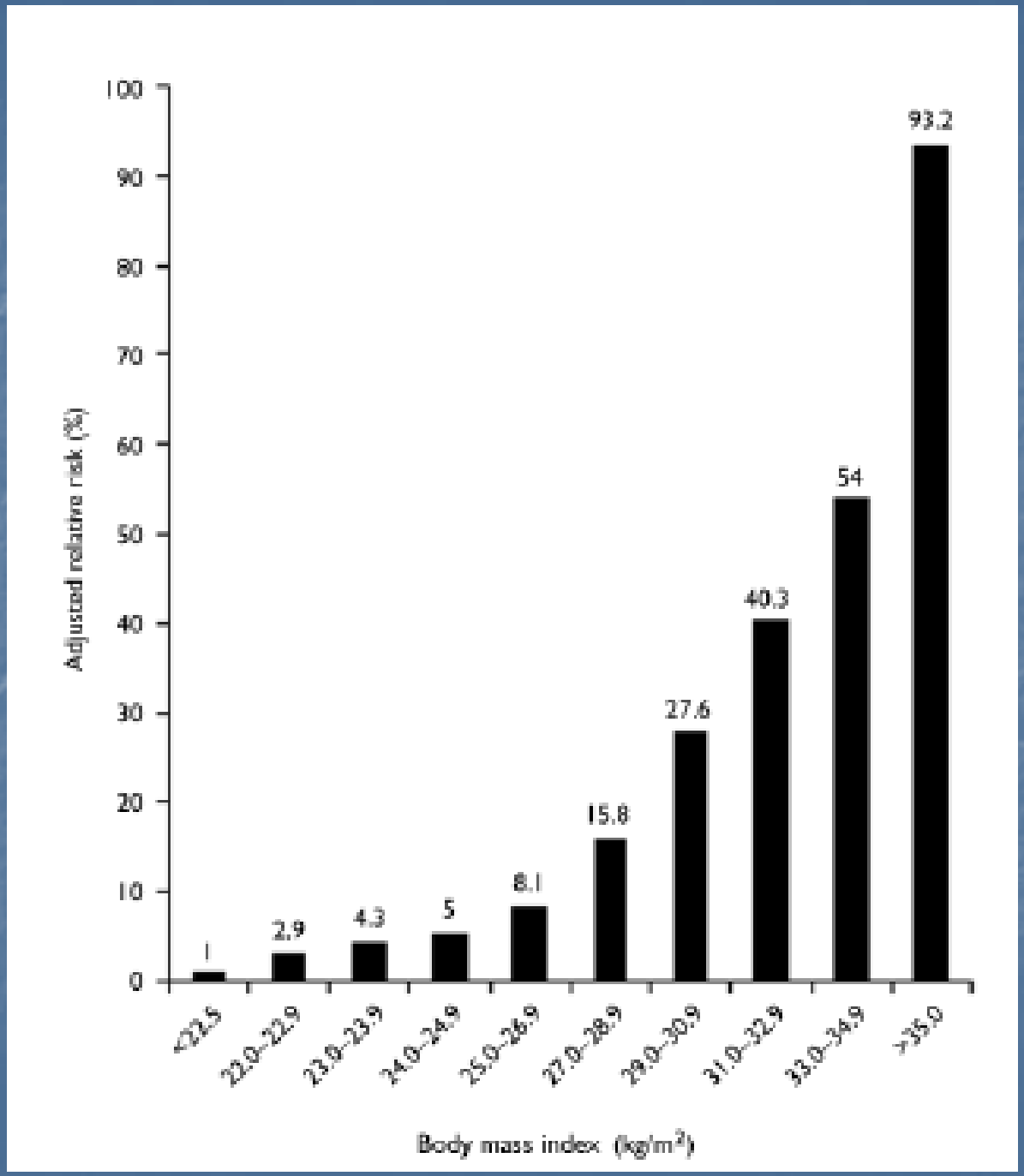
Relative Risk of Developing Diabetes



- Lower with more lifestyle factors
  - Moderate physical activity
  - Healthy diet
  - Never smoked
  - Moderate alcohol use
  - BMI<25
  - Waist circumference less than 88 cm for women or 92 cm for men

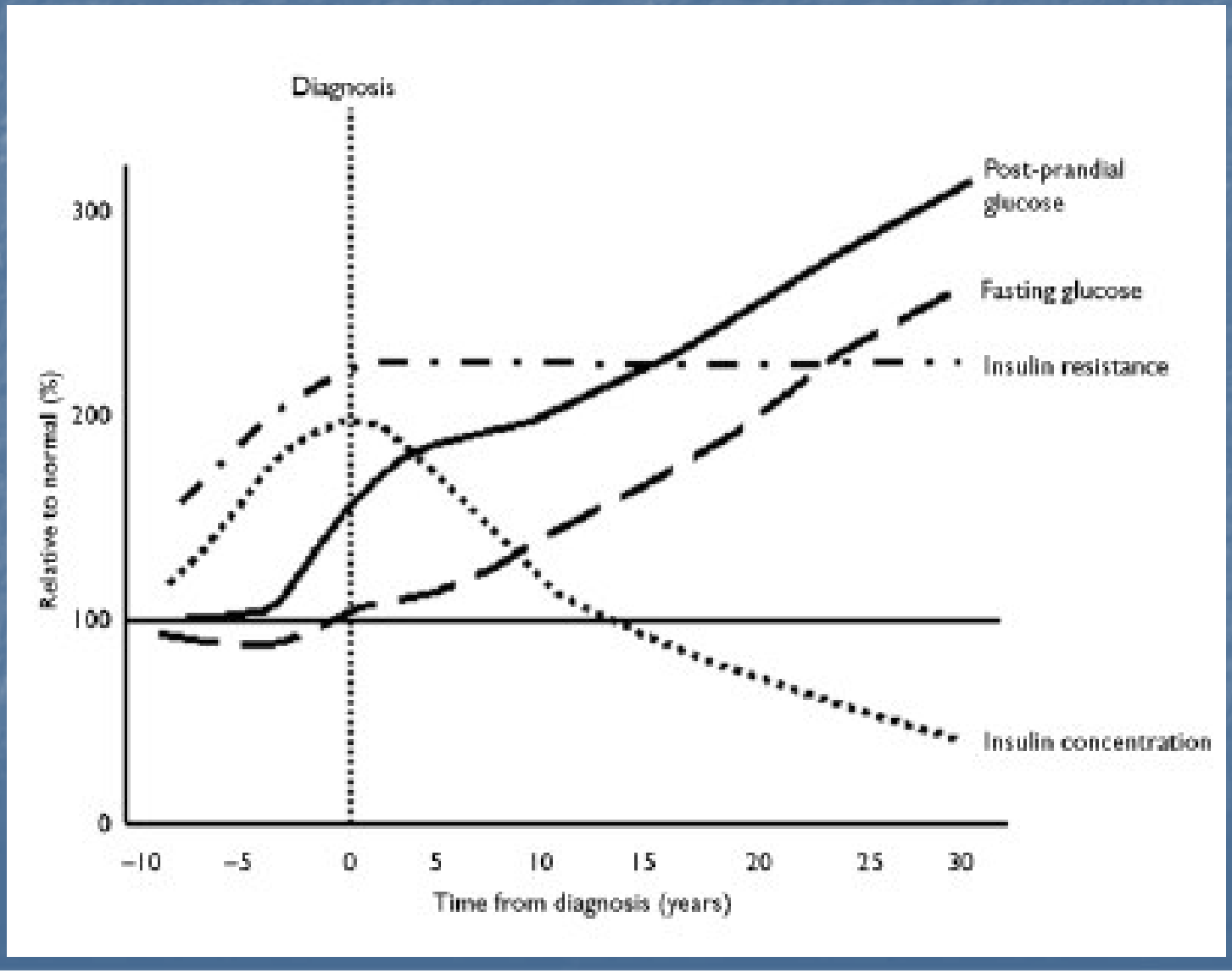
Mozaffarian D. Arch Intern Med 2009;169(8):798-807

BMI and Diabetes

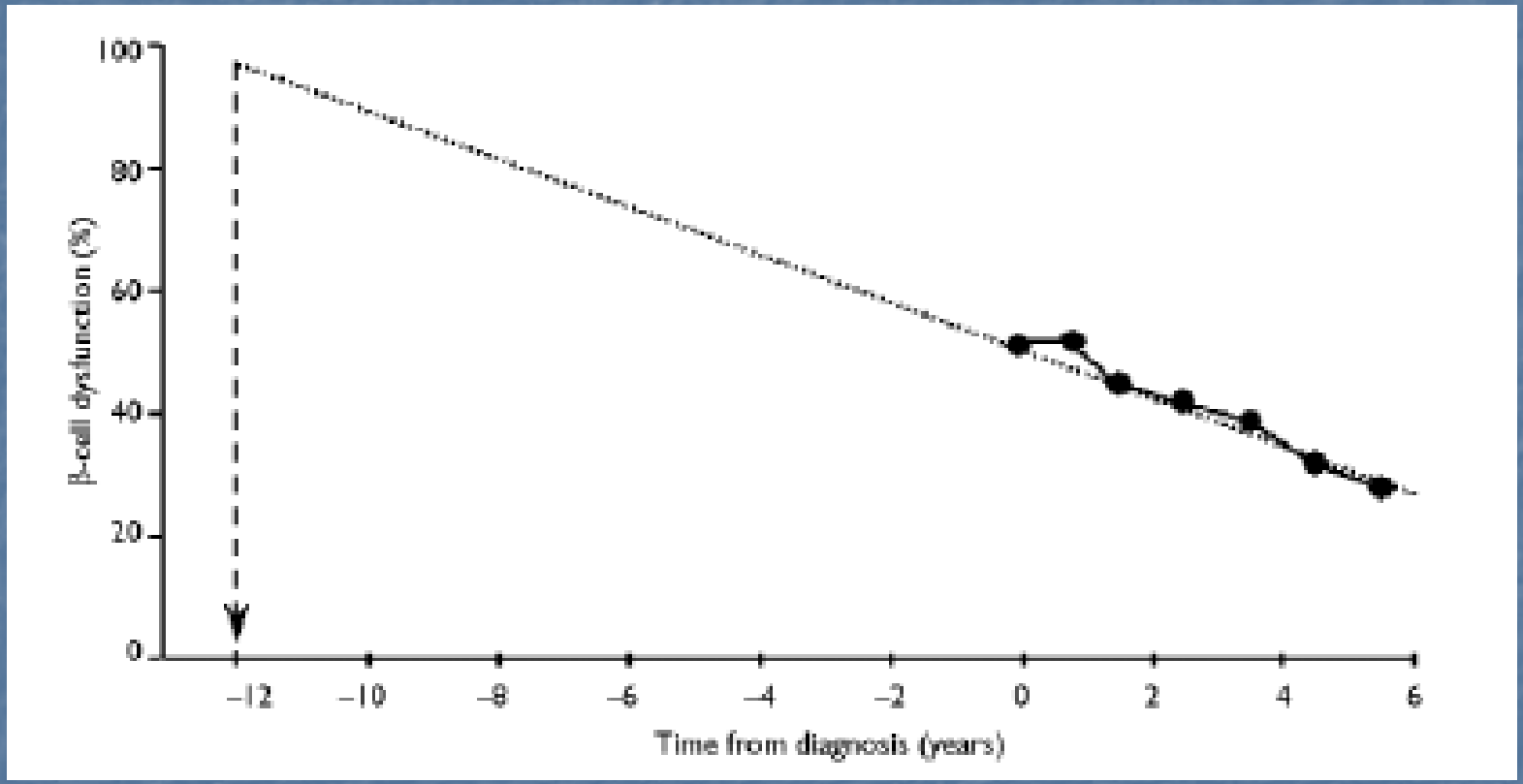


Colditz et al Ann Internal Med 1995; 122:481-486

β Cell Failure

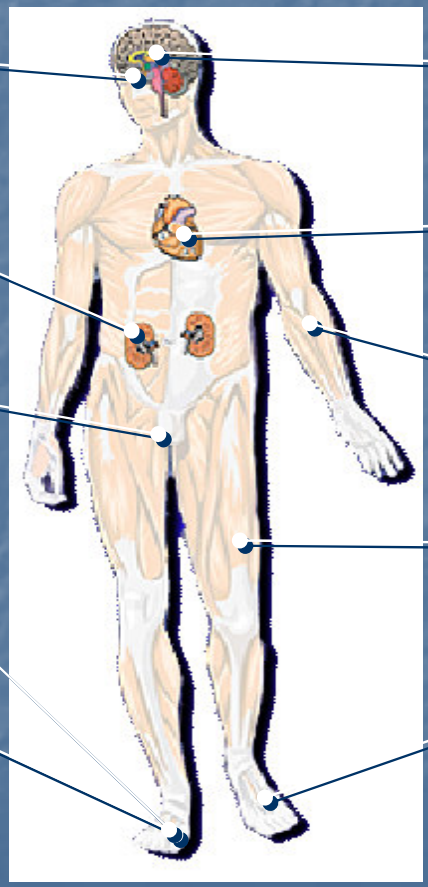


β Cell Failure



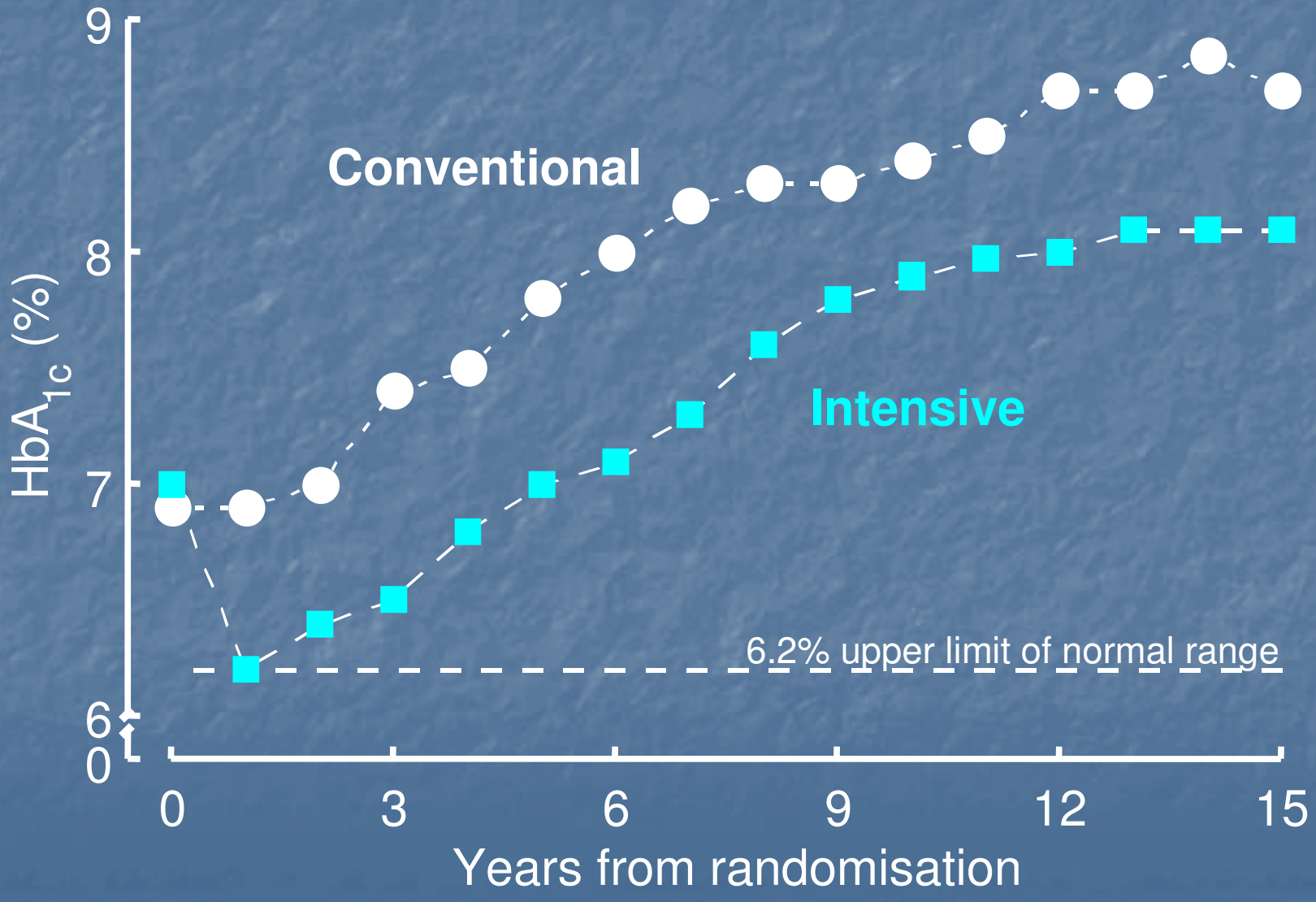
Holman et al Diab Res Clin Pract 1998;40:S21-S25

Vascular Complications Of Type 2 Diabetes At The Time Of Diagnosis



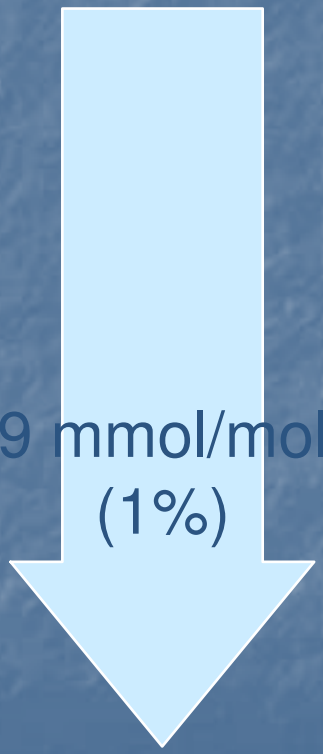
Retinopathy	21%	7%	Cerebrovascular disease
Nephropathy	18%	18%	Abnormal ECG
Erectile dysfunction	20%	35%	Hypertension
Ischaemic skin changes (foot)	6%	4.5%	Intermittent claudication
Abnormal vibration threshold (foot)	7%	13%	Absent foot pulses

UKPDS HbA_{1c} Median Values



Lessons from UKPDS: Better Control Means Fewer Complications

Every 9mmol/mol (1%) reduction in HbA_{1c}



	REDUCED RISK*
Deaths from diabetes	–21%
Heart attacks	–14%
Microvascular complications	–37%
Peripheral vascular disorders	–43%

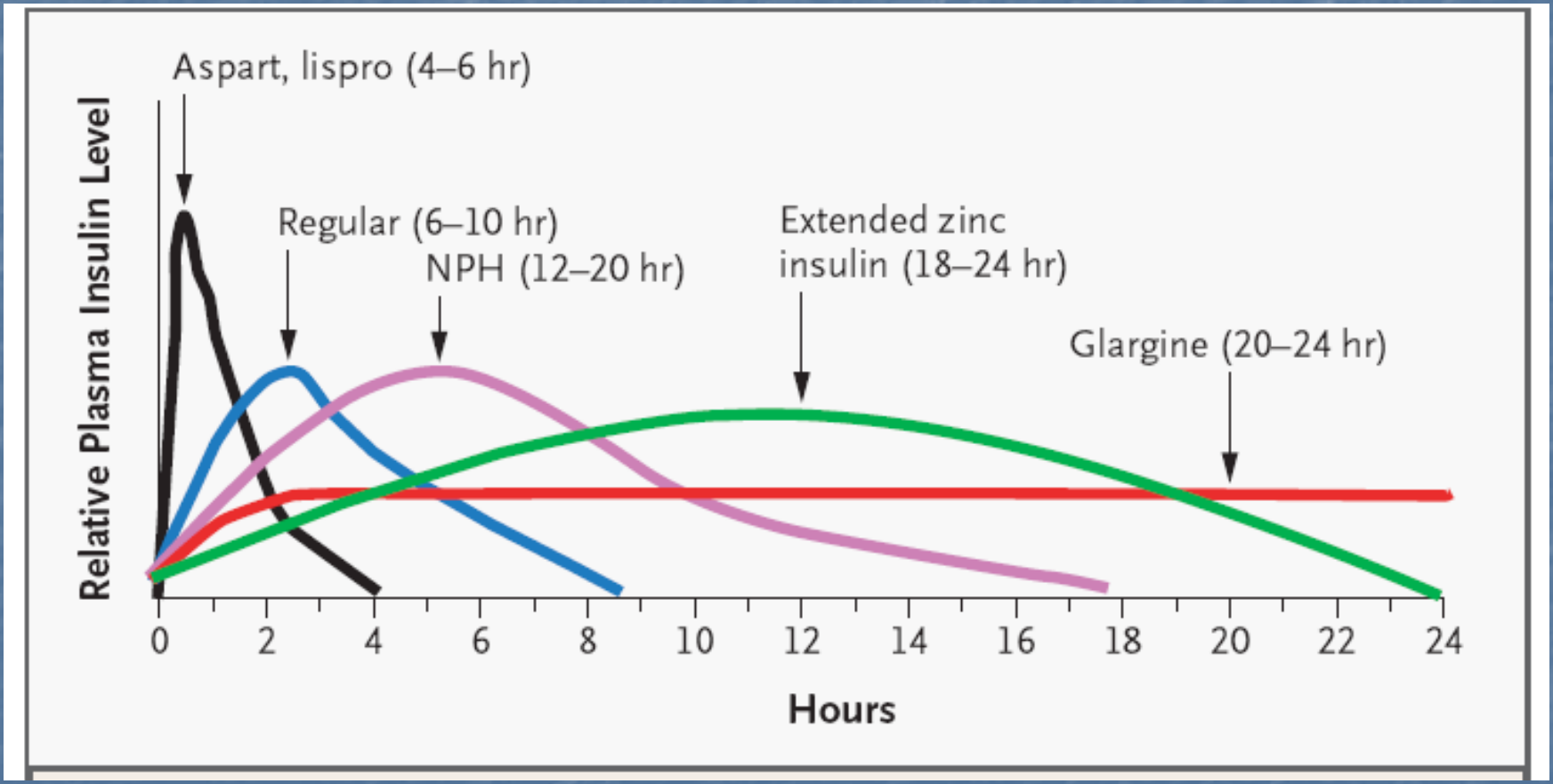
UKPDS 35. BMJ 2000;321:405–12

*p<0.0001

Non-Insulin Hypoglycaemic Agents

- α glucosidase inhibitors
- Metaglinides
- Metformin
- Sulphonylureas
- Thiazolidindiones
- GLP – 1 analogues
- DPP IV inhibitors
- (SGLT 2 inhibitors)

Insulin



Hirsch NEJM 2005;352 (2):174-183

In Summary

- Diabetes is very common, and type 2 diabetes is becoming commoner
- Good glycaemic control is important to help reduce the risk of developing the microvascular and macrovascular complications – or to reduce the risk of progression

Diabetes for Optometrists – An Introduction

Dr Ketan Dhatariya MBBS MSc MD MS FRCP
Consultant in Diabetes and Endocrinology
Norfolk and Norwich University Hospital NHS Trust

www.drketandhatariya.com